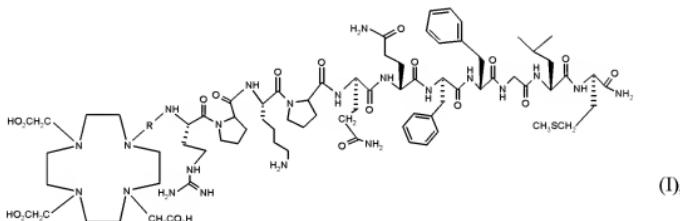


AMENDMENTS TO THE CLAIMS

Claim 1. (Withdrawn) A method of targeting a brain tumor, localizing or treating a brain tumor or a satellite lesion thereof in a host afflicted with brain tumor, comprising administering to the host a radio-nuclide labelled conjugate of substance P and a chelator molecule, having the abbreviation

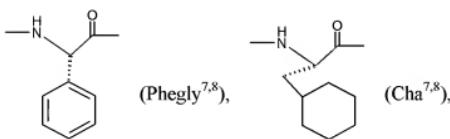
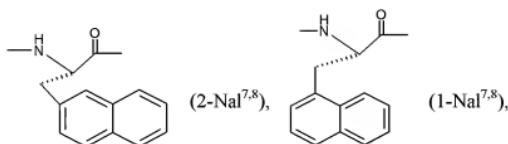
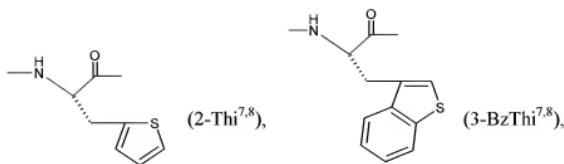
Chelator-R-Arg¹-Pro²-Lys³-Pro⁴-Gln⁵-Gln⁶-Phe⁷-Phe⁸-Gly⁹-Leu¹⁰-Met¹¹-NH₂ and the structure of formula I



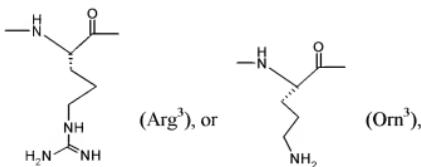
wherein

R is -CH₂-C(O)-, -CH(CO₂H)CH₂CH₂-C(O)- or -CH(CO₂H)CH₂-C(O)-,
or an analogue of formula I with at least one of the following modifications in the amino acid sequence of substance P:

- a) replacement of Met¹¹ by -NH-CH(CH₂CH₂-SO₂-CH₃)-C(O)- (hereinafter abbreviated Met(O₂)¹¹),
-NH-CH(CH₂CH₂-SO-CH₃)-C(O)- (hereinafter abbreviated Met(O)¹¹), or -NH-CH[CH(CH₃)CH₂CH₃]-C(O)- (hereinafter abbreviated Ile¹¹),
- b) replacement of Leu¹⁰ by -NH-CH[CH(CH₃)CH₂CH₃]-C(O)- (hereinafter abbreviated Ile¹⁰),
- c) replacement of Gly⁹ by -N(CH₃)-CH₂-C(O)- (hereinafter abbreviated Sar⁹),
- d) replacement of Phe⁷ or Phe⁸ or both Phe⁷ and Phe⁸ by a residue of formulae



e) replacement of Lys³ by residue of formulae



f) truncation of 1 to 5 amino acids of the sequence Arg¹-Pro²-Lys³-Pro⁴-Gln⁵, or

g) replacement of 1 to 5 amino acids of the sequence Arg¹-Pro²-Lys³-Pro⁴-Gln⁵ by - N(CH₃)-CH₂-C(O)- (hereinafter abbreviated Sar), and wherein the conjugate is labelled with a radio-nuclide selected from the group consisting of Actinium-225, Bismut-212, Bismut-213, Lead-203, Copper-64, Copper-67, Gallium-66, Gallium-67, Gallium-68, Lutetium-177, Indium-111, Indium-113, Yttrium-86 and Yttrium-90, Dysprosium-162, Dysprosium-165, Dysprosium-167, Holmium-166, Praseodymium-142, Praseodymium-143, Promethium-149, and Terbium-149.

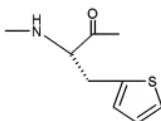
Claim 2. (Withdrawn) The method according to claim 1, wherein the amino acid sequence of substance P is:

- a) Arg-Pro-Lys-Pro-Gln-Gln-Phe-Phe-Gly-Leu-Met-NH₂,
- b) Arg-Pro-Lys-Pro-Gln-Gln-Phe-Phe-Gly-Leu-Met(O₂)-NH₂,
- c) Arg-Pro-Lys-Pro-Gln-Gln-Phe-Phe-Sar-Leu-Met-NH₂,
- d) Arg-Pro-Lys-Pro-Gln-Gln-Phe-Thi-Gly-Leu-Met-NH₂,
- e) Arg-Pro-Lys-Pro-Gln-Gln-Thi-Phe-Gly-Leu-Met-NH₂,
- f) Arg-Pro-Lys-Pro-Gln-Gln-Phe-Phe-Sar-Leu-Met(O₂)-NH₂,
- g) Arg-Pro-Lys-Pro-Gln-Gln-Phe-Thi-Gly-Leu-Met(O₂)-NH₂,
- h) Arg-Pro-Lys-Pro-Gln-Gln-Thi-Phe-Gly-Leu-Met(O₂)-NH₂,
- i) Arg-Pro-Lys-Pro-Gln-Gln-Phe-Thi-Sar-Leu-Met(O₂)-NH₂,
- j) Arg-Pro-Lys-Pro-Gln-Gln-Thi-Phe-Sar-Leu-Met-NH₂,
- k) Arg-Pro-Lys-Pro-Gln-Gln-Thi-Phe-Sar-Leu-Met(O₂)-NH₂
- l) Arg-Pro-Lys-Pro-Gln-Gln-Thi-Thi-Sar-Leu-Met-NH₂,
- m) Arg-Pro-Lys-Pro-Gln-Gln-Thi-Thi-Sar-Leu-Met(O₂)-NH₂,
- n) Arg-Pro-Lys-Pro-Gln-Gln-Thi-Thi-Gly-Leu-Met-NH₂, or
- o) Arg-Pro-Lys-Pro-Gln-Gln-Thi-Thi-Gly-Leu-Met(O₂)-NH₂.

Claim 3. (Withdrawn) The method according to claim 1, wherein the compound of formula I comprises in the 11-position of the amino acid sequence of the substance P a methionine sulfone residue of formula -NH-CH(CH₂CH₂-SO₂-CH₃)-C(O)- instead of a methionine residue.

Claim 4. (Withdrawn) The method according to claim 1, wherein the glycine residue in position 9 of the amino acid sequence of the substance P is replaced by a sarcosine residue of formula -N(CH₃)-CH₂-C(O)-.

Claim 5. (Withdrawn) The method according to claim 1, wherein the phenylalanine residue in the 7- or 8-position or in both said positions of the amino acid sequence of substance P is replaced by a 3-(2-thienyl)-alanine residue of formula



Claim 6. (Withdrawn) The method according to claim 1, wherein the phenylalanine residue in the 8-position of the amino acid sequence of substance P is replaced by a 3-(2-thienyl)-alanine and the glycine residue in position 9 is replaced by a sarcosine residue.

Claim 7. (Withdrawn) The method according to claim 1, wherein the methionine residue in the 11-position of the amino acid sequence of substance P is replaced by a methionine sulfone residue, and the phenylalanine residue in the 8-position is replaced by a 3-(2-thienyl)-alanine residue, or the glycine residue in position 9 is replaced by a sarcosine residue.

Claim 8. (Withdrawn) The method according to claim 1, wherein the amino acid sequence in formula I is:

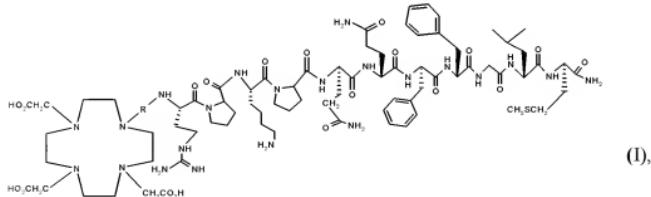
- a) Arg-Pro-Lys-Pro-Gln-Gln-Phe-Phe-Gly-Leu-Met(O₂)-NH₂,
- b) Arg-Pro-Lys-Pro-Gln-Gln-Phe-Phe-Sar-Leu-Met-NH₂,
- c) Arg-Pro-Lys-Pro-Gln-Gln-Phe-Thi-Gly-Leu-Met-NH₂,
- d) Arg-Pro-Lys-Pro-Gln-Gln-Thi-Phe-Gly-Leu-Met-NH₂,
- e) Arg-Pro-Lys-Pro-Gln-Gln-Phe-Phe-Sar-Leu-Met(O₂)-NH₂,
- f) Arg-Pro-Lys-Pro-Gln-Gln-Phe-Thi-Gly-Leu-Met(O₂)-NH₂,
- g) Arg-Pro-Lys-Pro-Gln-Gln-Thi-Thi-Gly-Leu-Met-NH₂, or
- h) Arg-Pro-Lys-Pro-Gln-Gln-Phe-Thi-Sar-Leu-Met(O₂)-NH₂.

Claim 9. (Withdrawn) The method according to claim 1, wherein the amino acid sequence in formula I is:

- a) Arg-Pro-Lys-Pro-Gln-Gln-Phe-Phe-Sar-Leu-Met(O₂)-NH₂, or
- b) Arg-Pro-Lys-Pro-Gln-Gln-Phe-Thi-Gly-Leu-Met(O₂)-NH₂.

Claim 10. (Withdrawn) A method of targeting a brain tumor, localizing or treating a brain tumor or a satellite lesion thereof in a host afflicted with brain tumor, which comprises administering to the host at least one conjugate of substance P and a chelator molecule, having the abbreviation

Chelator-R-Arg¹-Pro²-Lys³-Pro⁴-Gln⁵-Gln⁶-Phe⁷-Phe⁸-Gly⁹-Leu¹⁰-Met¹¹-NH₂ and the structure of formula I



wherein

R is -CH₂-C(O)-, -CH(CO₂H)CH₂CH₂-C(O)- or -CH(CO₂H)CH₂-C(O)-,

or an analogue of formula I with at least one of the following modifications in the amino acid sequence of substance P:

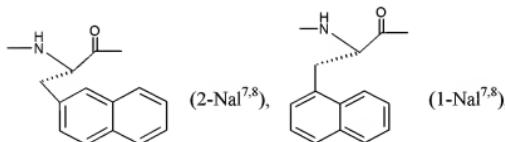
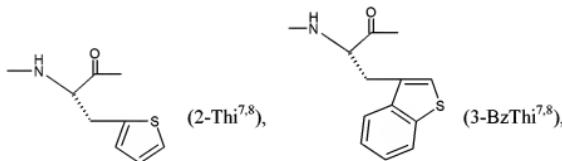
a) replacement of Met¹¹ by -NH-CH(CH₂CH₂-SO₂-CH₃)-C(O)- (hereinafter abbreviated Met(O₂)¹¹),

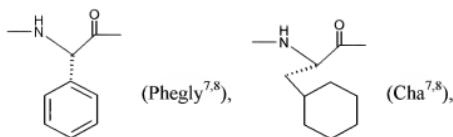
-NH-CH(CH₂CH₂-SO-CH₃)-C(O)- (hereinafter abbreviated Met(O)¹¹), or -NH-CH[CH(CH₃)CH₂CH₃]-C(O)- (hereinafter abbreviated Ile¹¹),

b) replacement of Leu¹⁰ by -NH-CH[CH(CH₃)CH₂CH₃]-C(O)- (hereinafter abbreviated Ile¹⁰),

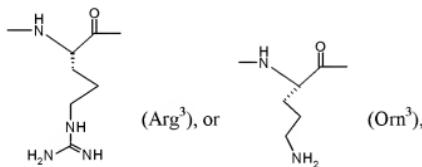
c) replacement of Gly⁹ by -N(CH₃)-CH₂-C(O)- (hereinafter abbreviated Sar⁹),

d) replacement of Phe⁷ or Phe⁸ or both Phe⁷ and Phe⁸ by a residue of formulae





e) replacement of Lys³ by residue of formulae

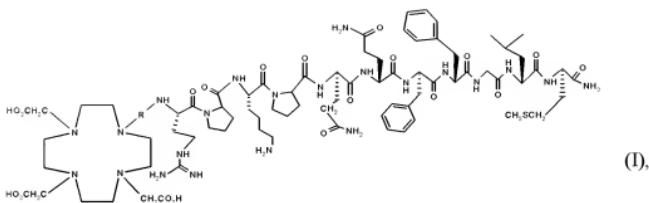


f) truncation of 1 to 5 amino acids of the sequence Arg¹-Pro²-Lys³-Pro⁴-Gln⁵, or

g) replacement of 1 to 5 amino acids of the sequence Arg¹-Pro²-Lys³-Pro⁴-Gln⁵ by -N(CH₃)-CH₂-C(O)- (hereinafter abbreviated Sar).

Claim 11. (Withdrawn) A therapeutic or diagnostic method for targeting a brain tumor, localizing or treating a brain tumor or a satellite lesion thereof in a mammal, comprising administering to a mammal in need of such therapy, an effective amount of a radio-nuclide labelled conjugate of substance P and a chelator molecule, having the abbreviation

Chelator-R-Arg¹-Pro²-Lys³-Pro⁴-Gln⁵-Gln⁶-Phe⁷-Phe⁸-Gly⁹-Leu¹⁰-Met¹¹-NH₂ and the structure of formula I

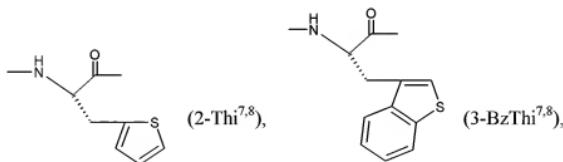


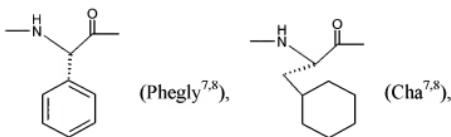
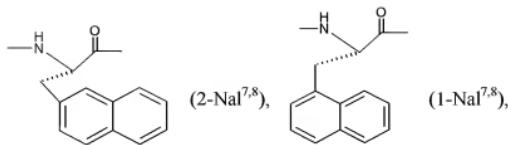
wherein

R is -CH₂-C(O)-, -CH(CO₂H)CH₂CH₂-C(O)- or -CH(CO₂H)CH₂-C(O)-,

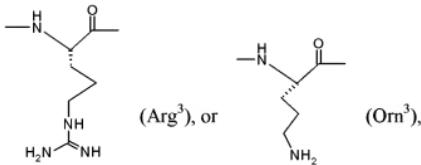
or an analogue of formula I with at least one of the following modifications in the amino acid sequence of substance P:

- replacement of Met¹¹ by -NH-CH(CH₂CH₂-SO₂-CH₃)-C(O)- (hereinafter abbreviated Met(O₂)¹¹),
-NH-CH(CH₂CH₂-SO₂-CH₃)-C(O)- (hereinafter abbreviated Met(O)¹¹), or -NH-CH[CH(CH₃)CH₂CH₃]-C(O)- (hereinafter abbreviated Ile¹¹),
- replacement of Leu¹⁰ by -NH-CH[CH(CH₃)CH₂CH₃]-C(O)- (hereinafter abbreviated Ile¹⁰),
- replacement of Gly⁹ by -N(CH₃)-CH₂-C(O)- (hereinafter abbreviated Sar⁹),
- replacement of Phe⁷ or Phe⁸ or both Phe⁷ and Phe⁸ by a residue of formulae





e) replacement of Lys³ by residue of formulae



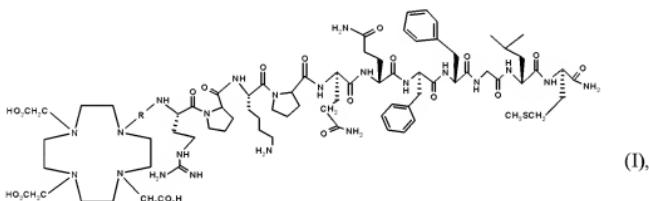
f) truncation of 1 to 5 amino acids of the sequence Arg¹-Pro²-Lys³-Pro⁴-Gln⁵, or

g) replacement of 1 to 5 amino acids of the sequence Arg¹-Pro²-Lys³-Pro⁴-Gln⁵ by -N(CH₃)-CH₂-C(O)- (hereinafter abbreviated Sar),

and wherein the conjugate is labelled with a radio-nuclide selected from the group consisting of Actinium-225, Bismut-212, Bismut-213, Lead-203, Copper-64, Copper-67, Gallium-66, Gallium-67, Gallium-68, Lutetium-177, Indium-111, Indium-113, Yttrium-86 and Yttrium-90, Dysprosium-162, Dysprosium-165, Dysprosium-167, Holmium-166, Praseodymium-142, Praseodymium-143, Promethium-149, and Terbium-149.

Claim 12. (Withdrawn) A method of delivering a radio-nuclide labelled substance P conjugate of formula I or an analogue thereof to a host, comprising administering to a host a radio-nuclide labelled conjugate of substance P and a chelator molecule, having the abbreviation

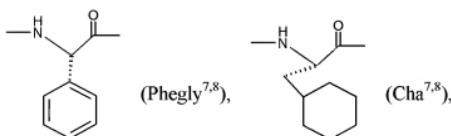
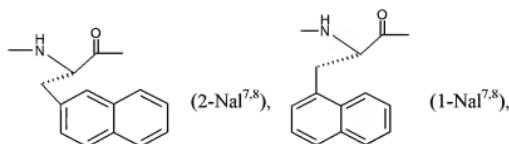
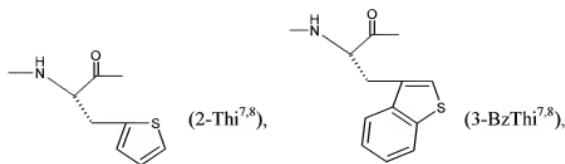
Chelator-R-Arg¹-Pro²-Lys³-Pro⁴-Gln⁵-Gln⁶-Phe⁷-Phe⁸-Gly⁹-Leu¹⁰-Met¹¹-NH₂ and the structure of formula I



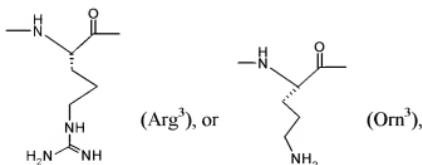
wherein

R is -CH₂-C(O)-, -CH(CO₂H)CH₂CH₂-C(O)- or -CH(CO₂H)CH₂-C(O)-,
or an analogue of formula I with at least one of the following modifications in the amino acid sequence of substance P:

- a) replacement of Met¹¹ by -NH-CH(CH₂CH₂-SO₂-CH₃)-C(O)- (hereinafter abbreviated Met(O₂)¹¹),
-NH-CH(CH₂CH₂-SO-CH₃)-C(O)- (hereinafter abbreviated Met(O)¹¹), or -NH-CH[CH(CH₃)CH₂CH₃]-C(O)- (hereinafter abbreviated Ile¹¹),
- b) replacement of Leu¹⁰ by -NH-CH[CH(CH₃)CH₂CH₃]-C(O)- (hereinafter abbreviated Ile¹⁰),
- c) replacement of Gly⁹ by -N(CH₃)-CH₂-C(O)- (hereinafter abbreviated Sar⁹),
- d) replacement of Phe⁷ or Phe⁸ or both Phe⁷ and Phe⁸ by a residue of formulae



e) replacement of Lys³ by residue of formulae

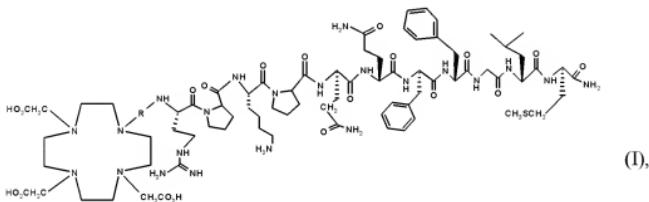


f) truncation of 1 to 5 amino acids of the sequence Arg¹-Pro²-Lys³-Pro⁴-Gln⁵, or

g) replacement of 1 to 5 amino acids of the sequence Arg¹-Pro²-Lys³-Pro⁴-Gln⁵ by -N(CH₃)-CH₂-C(O)- (hereinafter abbreviated Sar),
and wherein the conjugate is labeled with a radio-nuclide selected from the group consisting of Actinium-225, Bismut-212, Bismut-213, Lead-203, Copper-64, Copper-67, Gallium-66, Gallium-67, Gallium-68, Lutetium-177, Indium-111, Indium-113, Yttrium-86 and Yttrium-90, Dysprosium-162, Dysprosium-165, Dysprosium-167, Holmium-166, Praseodymium-142, Praseodymium-143, Promethium-149, and Terbium-149.

Claim 13. (Withdrawn) A method for the manufacture of a medicament useful for the detection and therapeutic treatment of a brain tumor or satellite lesion thereof in a mammal, which comprises mixing a radio-nuclide labelled conjugate of substance P and a chelator molecule, having the abbreviation

Chelator-R-Arg¹-Pro²-Lys³-Pro⁴-Gln⁵-Gln⁶-Phe⁷-Phe⁸-Gly⁹-Leu¹⁰-Met¹¹-NH₂ and the structure of formula I

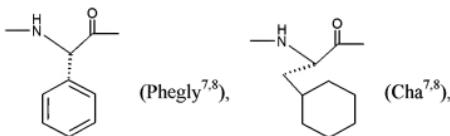
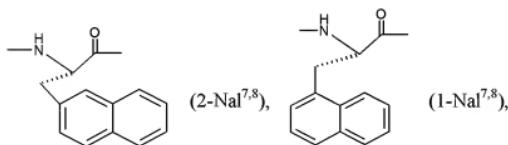
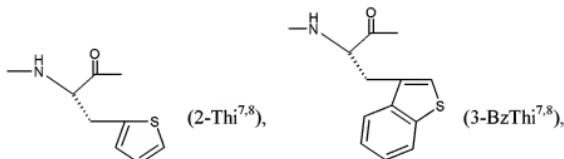


wherein

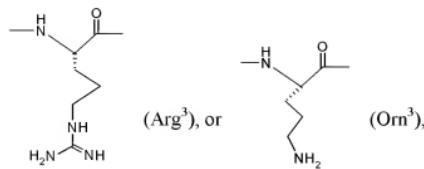
R is -CH₂-C(O)-, -CH(CO₂H)CH₂CH₂-C(O)- or -CH(CO₂H)CH₂-C(O)-,
or an analogue of formula I with at least one of the following modifications in the amino acid sequence of substance P:

a) replacement of Met¹¹ by -NH-CH(CH₂CH₂-SO₂-CH₃)-C(O)- (hereinafter abbreviated Met(O₂)¹¹),

- NH-CH(CH₂CH₂-SO-CH₃)-C(O)- (hereinafter abbreviated Met(O)¹¹), or -NH-CH[CH(CH₃)CH₂CH₃]-C(O)- (hereinafter abbreviated Ile¹¹),
- b) replacement of Leu¹⁰ by -NH-CH[CH(CH₃)CH₂CH₃]-C(O)- (hereinafter abbreviated Ile¹⁰),
- c) replacement of Gly⁹ by -N(CH₃)-CH₂-C(O)- (hereinafter abbreviated Sar⁹),
- d) replacement of Phe⁷ or Phe⁸ or both Phe⁷ and Phe⁸ by a residue of formulae



- e) replacement of Lys³ by residue of formulae



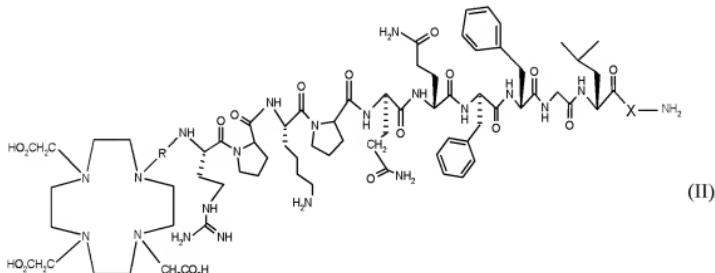
f) truncation of 1 to 5 amino acids of the sequence Arg¹-Pro²-Lys³-Pro⁴-Gln⁵, or
g) replacement of 1 to 5 amino acids of the sequence Arg¹-Pro²-Lys³-Pro⁴-Gln⁵ by -N(CH₃)-CH₂-C(O)- (hereinafter abbreviated Sar),
and wherein the conjugate is labelled with a radio-nuclide selected from the group consisting of Actinium-225, Bismut-212, Bismut-213, Lead-203, Copper-64, Copper-67, Gallium-66, Gallium-67, Gallium-68, Lutetium-177, Indium-111, Indium-113, Yttrium-86 and Yttrium-90, Dysprosium-162, Dysprosium-165, Dysprosium-167, Holmium-166, Praseodymium-142, Praseodymium-143, Promethium-149, and Terbium-149,

with a pharmaceutical carrier.

Claims 14-16. (Cancelled)

Claim 17. (Previously Presented) A conjugate of a substance P analogue and a chelator molecule, having the abbreviation

Chelator-R-Arg¹-Pro²-Lys³-Pro⁴-Gln⁵-Gln⁶-Phe⁷-Phe⁸-Gly⁹-Leu¹⁰-X¹¹-NH₂ and the structure of formula II



wherein

R is -CH₂-C(O)-, -CH(CO₂H)CH₂CH₂-C(O)- or -CH(CO₂H)CH₂-C(O)- and

X is -NH-CH(CH₂CH₂-SO₂-CH₃)-C(O)- (hereinafter abbreviated Met(O)¹¹), -NH-

CH(CH₂CH₂-SO-CH₃)-C(O)- (hereinafter abbreviated Met(O)¹¹), or -NH-

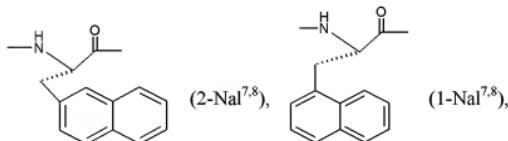
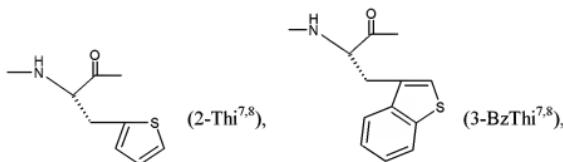
CH[CH(CH₃)CH₂CH₃]-C(O)- (hereinafter abbreviated Ile¹¹),

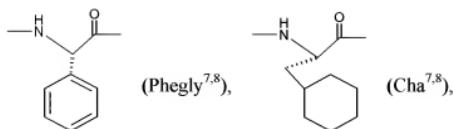
or an analogue of formula II with at least one of the following modifications in the amino acid sequence of substance P analogue:

a) replacement of Leu¹⁰ by -NH-CH(CH(CH₃)CH₂CH₃)-C(O)- (hereinafter abbreviated Ile¹⁰),

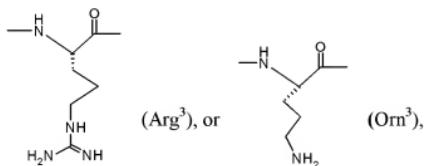
b) replacement of Gly⁹ by -N(CH₃)-CH₂-C(O)- (hereinafter abbreviated Sar⁹),

c) replacement of Phe⁷ or Phe⁸ or both Phe⁷ and Phe⁸ by a residue of formulae





d) replacement of Lys³ by residue of formulae



e) truncation of 1 to 5 amino acids of the sequence Arg¹-Pro²-Lys³-Pro⁴-Gln⁵, or
f) replacement of 1 to 5 amino acids of the sequence Arg¹-Pro²-Lys³-Pro⁴-Gln⁵ by
-N(CH₃)-CH₂-C(O)- (hereinafter abbreviated Sar),
and wherein the conjugate is unlabelled or labeled with a radio-nuclide selected from the group consisting of Actinium-225, Bismut-212, Bismut-213, Lead-203, Copper-64, Copper-67, Gallium-66, Gallium-67, Gallium-68, Lutetium-177, Indium-111, Indium-113, Yttrium-86 and Yttrium-90, Dysprosium-162, Dysprosium-165, Dysprosium-167, Holmium-166, Praseodymium-142, Praseodymium-143, Promethium-149, and Terbium-149.

Claim 18. (Previously Presented) The conjugate of claim 17 wherein
X is -NH-CH(CH₂CH₂-SO₂-CH₃)-C(O)- (hereinafter abbreviated Met(O₂)¹¹).

Claim 19. (Previously Presented) A composition comprising at least one pharmaceutical carrier and at least one conjugate according to claim 17.

Claim 20. (Previously Presented) A composition comprising at least one pharmaceutical carrier and at least one conjugate according to claim 18.

Claim 21. (Withdrawn) A method of targeting a brain tumor or treating a brain tumor in a host afflicted with brain tumor, comprising administering to the host a conjugate of claim 17.

Claim 22. (Withdrawn) A method of targeting a glioma or treating a glioma in a host afflicted with glioma, comprising administering to the host a conjugate of claim 17.

Claim 23. (Withdrawn) A method of targeting a brain tumor or treating a brain tumor in a host afflicted with brain tumor, comprising administering to the host a conjugate of claim 18.

Claim 24. (Withdrawn) A method of targeting a glioma or treating a glioma in a host afflicted with glioma, comprising administering to the host a conjugate of claim 18.

Claim 25. (Withdrawn) The method of claim 21, wherein the conjugate is administered by loco-regional application to a tumor center or into a resection cavity of the host.

Claim 26. (Withdrawn) The method of claim 22, wherein the conjugate is administered by loco-regional application to a tumor center or into a resection cavity of the host.

Claim 27. (Withdrawn) The method of claim 23, wherein the conjugate is administered by loco-regional application to a tumor center or into a resection cavity of the host.

Claim 28. (Withdrawn) The method of claim 24, wherein the conjugate is administered by loco-regional application to a tumor center or into a resection cavity of the host.

Claim 29. (Currently Amended) A method for the manufacture of a radiopharmaceutical or radiodiagnostic formulation useful for targeting a brain tumor or

treating a brain tumor in a host afflicted with brain tumor, which comprises a radio-nuclide labeled conjugate of claim 17

- (a) preparing a suitable substance P analogue in a side chain protected form by solid phase peptide synthesis;
- (b) coupling the side chain protected substance P analogue with a prochelator selected from the group consisting of DOTAGA('Bu)₄, DOTASA('Bu)₄, and DOTA('Bu)₃ to obtain a protected conjugate;
- (c) cleaving the protected conjugate from resin and removing the protection groups to obtain an unlabelled conjugate of claim 17; and
- (d) labeling the unlabelled conjugate with a radionuclide to obtain a labeled conjugate of claim 17.

Claim 30. (Currently Amended) A method for the manufacture of a radiopharmaceutical or radiodiagnostic formulation useful for targeting a brain tumor or treating a brain tumor in a host afflicted with brain tumor, which comprises a radio-nuclide labeled conjugate of claim 18

- (a) preparing a suitable substance P analogue in a side chain protected form by solid phase peptide synthesis;
- (b) coupling the side chain protected substance P analogue with a prochelator selected from the group consisting of DOTAGA('Bu)₄, DOTASA ('Bu)₄, and DOTA ('Bu)₃ to obtain a protected conjugate;
- (c) cleaving the protected conjugate from resin and removing the protection groups to obtain an unlabelled conjugate of claim 18; and
- (d) labeling the unlabelled conjugate with a radionuclide to obtain a labeled conjugate of claim 18.